

Docket No.: 7049405002
Customer No. 23,639

Application Serial No. 09/575,377

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Amendments to the Claims:

Claims 1 - 50 (cancelled)

51. (Currently amended) A method for identifying one or more ion channels of a cell that may be affected by a test substance by deconvoluting a change in cell membrane potential, comprising:

exposing a test substance to a system device and accompanying software,
in which said system device comprises:

(a) a solid state microelectrode array;
(b) a serum-free cell culture comprising one or more electrically active cells having a cell membrane including one or more ion channels, which cells are capable of providing a measurable action potential that exhibits changes in one or more perceptible characteristics selected from after potential, time to cessation of activity, frequency, amplitude, shape, spike rate, or time constant in response to a test substance;

(c) an intervening layer that is acting as a high impedance seal and which (i) comprises a surface modifying agent, and (ii) is positioned between said microelectrode and said one or more cells of said cell culture, that provides a high impedance seal with said one or more cells and allows a deconvolution step to be performed, and

(d) accompanying deconvolution software with instructions that can be implemented by a computer to deconvolute changes in the action potential of the and which relate changes in the characteristics exhibit by the action potential to one or more ion channels of said one or more cells upon exposure to the test substance, wherein the deconvolution analysis does not include a spectral analysis that makes use of a Fourier transformation, and

performing a deconvolution analysis to identify an ion channel affected by said test substance.

52. (Currently Amended) The method of claim 51, wherein the one or ore more characteristics exhibited by said action potential is manifested in its waveform or a derivative thereof.

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53. (Currently Amended) The method of claim 52, in which the one or more characteristics include at least one of ~~after-potential~~, time to cessation of activity, frequency, amplitude, or shape, ~~spike rate, or time constant~~.

54. (Previously Added) The method of claim 51, in which the instructions comprise data processing instructions capable of receiving input data comprising data on ion flux through ion channels selected from the group consisting of sodium channels, potassium channels, calcium channels, and combinations thereof.

55. (Currently Amended) The method ~~if~~ of claim 51, in which the microelectrode is planar or flexible.

56. (Previously Added) The method of claim 51, in which the microelectrode is a field effect transducer.

57. (Currently Amended) The method of claim 51, which further comprises an insulator layer ~~outside~~ surrounding the microelectrode selected from the group consisting of silicon, modified silicon dioxide, silicon nitride, silicon carbide, germanium, silica, gallium, arsenide, epoxy resin, polystyrene, polysulfone, alumina, silicone, fluoropolymer, polyester, acrylic copolymers, polylactate, or combinations thereof.

58. (Previously Added) The method of claim 51 in which said electrically active cell comprises a neuronal cell or a cardiac cell.

59. (Previously Added) The method of claim 58 in which the neuronal cell is a hippocampal cell.

60. (Previously Added) The method of claim 51 in which the cell culture comprises a stem cell, a transformed stem cell, their respective progeny, or a combination thereof.

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61. (Currently Amended) The method of claim 51 ~~40~~ in which the stem cell is exposed to a differentiating factor.
62. (Previously Added) The method of claim 51 in which the surface modifying agent comprises a self-assembling monolayer or monolayers.
63. (Previously Added) The method of claim 62 in which the self-assembling monolayer comprises a silane, a thiol, isocyanide, polyelectrolyte or combinations thereof.
64. (Previously Added) The method of claim 51, wherein the intervening layer further comprises cell anchorage molecules selected from the group consisting of antibodies, antigens, receptor ligands, receptors, lectins, carbohydrates, enzymes, enzyme inhibitors, biotin, avidin, streptavidin, RGD-type peptides, integrins, cadherins, modified lipids, and combinations thereof.
65. (Previously Added) The method of claim 51, wherein the intervening layer further comprises a high viscosity mixture comprising alcohols, ethers, esters, ketones, amides, glycols, amino acids, saccharides, carboxymethylsaccharides, carboxyethylsaccharides, aminosaccharides, acylaminosaccharides, polymers thereof, or combinations thereof.
66. (Previously Added) The method of claim 51 in which one or more cells are transfected with endogenous or exogenous nucleic acid.
67. (Previously Added) The method of claim 66 in which the nucleic acid comprises a nucleotide sequence associated with known or unknown function.
68. (Previously Added) The method of claim 51, wherein the cell culture is coated with a polymer.

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69. (Previously Added) The method of claim 68 in which the polymer comprises cellulose, methylcellulose, or dextran.

70. (Currently Amended) The method of claim ~~4~~ 51, wherein a second layer is in contact with the electrically active cells and is attractive to cell adherence.

71. (Previously Added) The method of claim 51 in which the test substance comprises a toxin, a drug, a pathogen, a neurotransmitter, a nerve agent, or mixtures thereof.

72. (Previously Added) The method of claim 51 in which the deconvolution of cell membrane potential includes deconvoluting the cell action potential or its derivative.

73. (Previously Added) The method of clam 72, in which deconvolution of the action potential or its derivatives provides information on pathways in the cell affected by the test substance.

74. (New) The method of claim 73, wherein said information on pathways in the cell involves reference to a data library of known compounds classified into one or more functional categories.